# Current best evidence from dermatology literature

**Paller AS, Mercy K, Kwasny MJ, Choon SE, Cordoro KM, Girolomoni G, *et al.* Association of pediatric psoriasis severity with excess and central adiposity: An international cross-sectional study. Arch Dermatol 2012;19:1-11.**

Psoriasis begins during childhood in 22-33% of the cases, and this incidence has increased to more than double, since the early 1970s. Adults with psoriasis have an increased risk of obesity, myocardial infarction, stroke, and diabetes mellitus. Recent studies also suggest the association of psoriasis with obesity in children. The objective of this study was to investigate the relationship of excess and central adiposity with pediatric psoriasis severity.

In this multicenter cross-sectional study, children (5-17 years) were enrolled from nine countries. Psoriasis was classified as mild psoriasis (MP) (worst physician's global assessment [PGA] score ≤3 with body surface area [BSA] ≤10%) or severe psoriasis (SP) (worst PGA score ≥3 with BSA >10%). Excess adiposity (body mass index [BMI] percentile) and central adiposity (waist circumference percentile and waist to height ratio) were evaluated.

A total of 614 children were enrolled from nine countries, and 205 age- and sex-matched children without inflammatory disorders served as controls. Excess adiposity (BMI ≥85$^{th}$ percentile) occurred in 155 (37.9%) psoriatic children versus 42 (20.5%) controls but did not differ significantly by severity. The odds ratio (OR) (95% confidence interval [CI]) of obesity (BMI ≥95$^{th}$ percentile) overall in psoriatic children versus controls was 4.29 (1.96-9.39) and was higher with SP (4.92; 2.20-10.99) than with MP (3.60; 1.56-8.30), particularly in the United States (7.60; 2.47-23.34, and 4.72; 1.43-15.56, respectively). Waist circumference above the 90$^{th}$ percentile occurred in 9.3% of the control, 14.0% of the MP, and 21.2% of the of SP participants internationally; this incidence too was highest in the US (12.0%, 20.8%, and 31.1%, respectively). Waist to height ratio was significantly higher in psoriatic (0.48) versus control (0.46) children but was unaffected by psoriasis severity. Children with SP at its worst, but mild at enrollment, showed no significant difference in excess or central adiposity from children whose psoriasis remained severe.

**Comments:** The prevalence of obesity has increased significantly over the past few years and obesity in children is also associated with increased risk of sleep apnea, cardiovascular risk factors, insulin resistance, orthopedic complications, and mortality resulting from cardiovascular disease in adulthood. This study has demonstrated that children with psoriasis have excess adiposity and increased central adiposity regardless of psoriasis severity. Most children with MP were overweight but not obese, while most children with SP were obese. The odds of obesity were 3.60 with MP 4.92 with SP globally however this was particularly high in the United States (OR, 6.61). The BMI percentile distributions showed increased adiposity in both American and European participants with MP and SP but only in children with MP from Asia. These ORs are considerably greater than those for adults in the United Kingdom and for metabolic syndrome in US adults with psoriasis of all severities suggesting a greater association of obesity and psoriasis with childhood-onset versus adult-onset psoriasis. Differences in diet and exercise between the American/European countries and Asia, as well as genetic variations, could account for regional variations in adiposity.

Both obesity and psoriasis are associated with overproduction of types 1 and 17 helper T-cell inflammatory cytokines. Although, association of obesity with psoriasis is clear but an unanswered question is whether high BMI is the precursor of psoriasis in children or whether psoriasis leads to an increased BMI percentile through chronic cytokine release from psoriatic tissue, compounded by a life-style that may favor excess adiposity (e.g., less physical activity and increased risk of depression).

**How to cite this article:** Narang T, Mahajan R. Current best evidence from dermatology literature. Indian J Dermatol Venereol Leprol 2013;79:448-52.

**Received:** February, 2013. **Accepted:** February, 2013. **Sources of Support:** Nil. **Conflict of Interest:** None declared.

The increased metabolic risks associated with excess and central adiposity warrant early monitoring and life-style modification. If more studies show excess adiposity to be a precursor for psoriasis, attempts at early weight loss and life-style modification will be important, not only to decrease the risk of metabolic disease but also to modulate the course of pediatric psoriasis.

### Rose AE, Goldberg DJ. Safety and efficacy of intradermal injection of botulinum toxin for the treatment of oily skin. Dermatol Surg 2013;39:443-8

Oily skin is one of the chief complaints of patients visiting dermatology out-patient. Although, various treatment modalities have been tried, they are generally unsatisfactory or associated with unacceptable side-effects. Some studies on botulinum toxin for the treatment of rhytides, have shown that acne occurred at a lower rate in treated patients than in those who received placebo which suggests that acetylcholine has a role in sebum production as well. The purpose of this study was to evaluate the safety and efficacy of intradermal injection of botulinum toxin A for the treatment of oily skin.

Twenty-five patients with oily skin were treated in the forehead region with intradermal injections 3-5 U of botulinum toxin given at 10 points. Baseline and post-treatment sebum production was measured using a sebometer. Photographs were taken. Patients were also asked to rate their satisfaction with the treatment in terms of improvement in their oily skin.

Treatment with botulinum toxin resulted in significantly lower sebum production at 1 week and subsequently at 1, 2, and 3 months after injection ($P < 0.001$). Twenty-three patients (91%) reported that they were satisfied (50-75% improvement) with intradermal botulinum toxin as a treatment for oily skin. The authors also observed a significant reduction in the pore size as well.

**Comments:** Excessive sebum production and enlarged pore size are a common complaint of the patients in the younger age group. Various treatment modalities like isotretinoin, topical retinoids, lasers, and peels have been used with varying effects. The most effective treatment for reducing sebum production is isotretinoin, but many patients cannot tolerate isotretinoin, are unwilling to accept the side-effects, or do not have severe enough disease to warrant its use. Sebum production is predominantly controlled by androgens and the role of the nervous system and acetylcholine in sebum production is not well-defined. Intradermal botulinum toxin may reduce sebum production through its neuromodulatory effects on the arrector pili muscles and the local muscarinic receptors in the sebaceous gland. Use of botulinum toxin in the management of pain has also led to speculation that botulinum toxin may work not only by blocking acetylcholine, but also by inhibiting the release of other neurotransmitters. Another limitation of currently available treatments for oily skin is that the treatment target, the sebaceous glands, are deeper in the dermis than many of the laser or resurfacing devices can reach. When targeting intradermal structures such as the sebaceous gland with toxin, the injection technique is critical because placement of the toxin too superficially will not be effective, and too deep an injection may lead to inadvertent paralysis of underlying skeletal muscle. Proper placement becomes even more important if treating oily skin on the cheeks or the perioral region because inadvertent paralysis in these areas can significantly affect function.

Intradermal botulinum toxin may be a viable alternative for patients who have oily skin. Intradermal injection of botulinum toxin significantly reduced sebum production in the forehead region, with a high degree of patient satisfaction. Intradermal botulinum toxin may also be useful as a primary or adjunctive treatment for enlarged pores. Further larger, randomized, blinded, placebo controlled studies are needed to assess the dose, frequency of injections and long-term adverse effects. Cost may also be a limiting factor in certain settings.

### Danby SG, Alenezi T, Sultan A, Lavender T, Chittock J, Brown K, *et al.* Effect of olive and sunflower seed oil on the adult skin barrier: Implications for neonatal skin care. Pediatr Dermatol 2013;30:42-50.

Application of emollients is regarded as a part of neonatal skin care all over the world, and also as a standard care in preventing and treating atopic dermatitis (AD). Regular use of emollient has a short- and long-term steroid sparing effect in mild to moderate AD. They may either act as occlusive agents (such as mineral oils) or humectants. The aim of this study was to ascertain the effect of olive oil and sunflower seed oil on the biophysical properties of the skin.

Nineteen adult subjects with and without a history of atopic dermatitis were recruited and randomized into two groups: The first group of 7 subjects applied six drops of olive oil to one forearm twice daily for 5 weeks and the second group of 12 subjects applied six drops of olive oil to one forearm and six drops of sunflower seed oil to the other twice daily for 4 weeks. The effect of the treatments was evaluated by determining stratum corneum integrity and cohesion, intercorneocyte cohesion, moisturization, skin surface pH, and erythema.

The authors noted that topical application of olive oil for 4 weeks caused a significant reduction in stratum corneum integrity and induced mild erythema in subjects with and without a history of AD. The decrease in skin barrier function (measured as basal transepidermal water loss) was significantly greater ($P = 0.04$) in subjects with a history of AD than in subjects with healthy skin. It caused a significant reduction in stratum corneum thickness on the skin damaged by tape stripping (akin to skin in AD). Sunflower seed oil, on the other hand preserved stratum corneum integrity, did not cause erythema, and improved hydration in the same volunteers.

**Comments:** Oils are important both in the routine care of the new-born as well as in the treatment of AD. These act by physically blocking the transepidermal water loss in stratum corneum and thereby increase the water content in the stratum corneum, thus producing a state of hydration. There are few studies that have proven the effectiveness of use of vegetable oils. However, there are not many studies comparing various oils. The present study shows that olive oil causes a significant reduction in stratum corneum integrity and thickness, does not significantly hydrate stratum corneum, and induces mild erythema in subjects with and without a history of AD. In comparison, sunflower seed oil promotes skin barrier integrity and hydration.

The ratio of oleic acid (OA) to linoleic acid (LA) in natural oils determines their effects on the skin. OA suppresses skin barrier homeostasis through its action on the N-methyl-D-aspartate cell-surface receptor expressed by epidermal keratinocytes whereas LA promotes skin barrier repair by activation of peroxisome proliferator-activated receptor-α. Oils with high LA and low OA content have the least propensity to cause irritant contact dermatitis. Olive oil contains 55-83% OA in contrast to sunflower seed oil in which LA is the predominant fatty acid.

This study has demonstrated that sunflower seed oil is a better emollient. In Indian context, further studies measuring the effect of coconut on skin barrier function and comparing them with olive oil and sunflower seed oil need to be undertaken as it is the most commonly used vegetable oil. Moreover, olive oil is costlier compared to coconut oil.

### Salem A, Nofal A, Hosny D. Treatment of common and plane warts in children with topical viable bacillus calmette-guerin. Pediatr Dermatol 2013;30:60-3.

Treatment of warts can be difficult especially in children as most of the destructive treatment modalities are painful, not universally effective and may lead to scarring/pigmentation. Immunotherapy with intralesional injections with bacillus calmette-guerin (BCG) or MW vaccine is another useful modality as it acts by augmenting cellular immune response against human papillomavirus, however, repeated/multiple painful injections may not be acceptable to the parents/children. The aim of this study was to evaluate the efficacy and safety of topical application of viable BCG in a paste formula as a new immunotherapeutic modality in the treatment of common and plane warts in children.

The present study recruited 80 children (3-14 years) with common and plane warts at different sites on the body. They were divided in to two groups: The first group of 40 patients received topical viable BCG paste and the control group of 40 patients received topical saline. BCG was applied once weekly for 6 consecutive weeks. Follow-up was at 6 months to detect any recurrences. The response to treatment was categorized as complete (disappearance of all lesions), partial (≥50% decrease in number), minimal (less than 50%), or none.

Of the 37 children in topical BCG group who completed the study, there was complete response in 13 patients (65%), partial response in 4 patients (20%), and no response in 2 patients (10%) with common warts and complete response in 9 patients (45%), partial response in 4 patients (20%), and no response in 5 patients (25%) with plane warts. A highly significant difference was found between the therapeutic response of common and plane warts to BCG and saline (placebo) ($P < 0.001$). No response was detected

in the control group. No recurrences or side-effects were observed in the BCG group.

**Comments:** Treatment of warts in children is a challenge for dermatologists due to the pain associated with the destructive therapies, variable success rate and recurrences. The present study has shown presents topical BCG application as a novel and effective therapeutic option for the treatment of warts in children. Topical BCG immunotherapy acts by causing the activation of CD4 lymphocytes and an increase in cytokines such as interleukin (IL)-1, IL-2, and tumor necrosis factor-alpha which have known anti-viral effect. This study demonstrates a significant difference between the therapeutic response of BCG paste over placebo both in common warts (65% vs. 0%) and plane warts (45% vs. 0%). Equally, important is the observation that there were no adverse events in the treatment group with none of the children experiencing any pain.

The authors based their study on the observations made in earlier studies where topical BCG application produced clearance in genital warts. It is well-known that viable BCG vaccine or intralesional mumps, measles, and rubella vaccine have been used as immunotherapy in warts. However, these are associated with injection site pain and with mild to moderate influenza like symptoms. Such adverse effects were not observed in the present study. However, there are few queries, which may require further clarification in future studies. According to the authors, the concentration of salicylic acid (an agent which in high concentration is used for treating warts) used in the BCG paste was subtherapeutic. However, it would be better to have a control group using a paste containing similar concentration of salicylic acid. Secondly, the authors mention that mixing BCG (a live attenuated vaccine) with such a low concentration of salicylic acid does not impair the growth and viability of BCG.

### Tan ST, Itinteang T, Day DJ, O'Donnell C, Mathy JA, Leadbitter P. Treatment of infantile haemangioma with captopril. Br J Dermatol 2012;167:619-24.

Infantile hemangioma (IH) is a common tumor of infancy, majority of the hemangiomas involute spontaneously, however, 10-15% of the hemangiomas require treatment because of the threat to life or function, or tissue distortion or destruction. The mainstay of management is pharmacological therapy that includes steroids and beta blockers like propranolol. Recent studies have reported that IH is an aberrant proliferation and differentiation of a primitive mesoderm-derived hemogenic endothelium regulated by the renin-angiotensin system (RAS). β-Blockers mediate their effect by the modulation of the RAS through inhibition of renin activity, so angiotensin converting enzyme (ACE) may be considered a potential therapeutic target.

In this study, the authors have presented the initial results of their open-labeled observational clinical trial using captopril, an ACE inhibitor (ACEi), in the treatment of problematic proliferating IH.

Two boys and six girls aged 5-22 weeks (mean 12.9) with problematic IH were recruited with the lesions located in nasal tip ($n$ = 1), cervicofacial ($n$ = 3), periorbital ($n$ = 1) and perineal ($n$ = 2) areas, and shoulder ($n$ = 1). After initial screening investigations, infants were admitted for initiation of captopril with a 0.1 mg/kg test dose orally, followed by 0.15 mg/kg once in 8 h over 24 h. This was then followed by dose escalation to 0.3 mg/kg once in 8 h for another 24 h. The dosage was increased to 0.5 mg/kg once in 8 h 1 week later, if a noticeable involution had not already occurred. The maximum dose limit was 1.5 mg/kg. The response of IH to captopril was documented clinically and photographically before and after treatment and any side effect was recorded. Transient mild renal impairment occurred in one subject but resolved spontaneously. No other complication was observed. The IHs in all patients responded to captopril at a dosage of 1.5 mg kg daily which led to a dramatic response in three, moderate response in two, and slow response in three patients. Continued involution of IHs was observed during the follow-up period of 8-19 months (mean 15.8) in all subjects. Treatment was ceased at 14 months of age in seven patients with no rebound growth. In one patient although, rapid healing of a large ulcerated retroauricular lesion was observed after 5.5 months of treatment, however, the lesion was excised to address its persistent distortion of the ear.

**Comments:** Although, β-blockers have become a mainstay of treatment, since their serendipitous discovery; we have to be careful about the side effects such as bradycardia, hypotension, hypoglycemia, and bronchospasm especially, in premature infants. The exact mechanism of action of propranolol in IH is also not known. It was hypothesized that renin drives

hemangioma proliferation and that β-blockers suppress renin activity by decreasing ACE. This theory suggests that ACEi and other angiotensin receptor-blocking drugs may have a role in the treatment of proliferating IH by inhibiting angiogenesis and vasculogenesis. The use of captopril for cardiac failure in infants has been well documented for over 20 years with a maximum dosage of 2 mg/kg thrice daily. Even though side effects such as renal insufficiency, oliguria, and hypotension are observed, but they are usually reversible with dose reduction. Captopril should also be started under supervision taking care of the hypotension and renal impairment but it appeared relatively safe in the small cohort observed in this study. The response of IH to an ACEi supports a critical role for the RAS in IH and represents a paradigm shift in the understanding and treatment of this enigmatic condition.

We will need more studies involving greater number of subjects, higher dose of captopril, longer follow-up or may be combination of β-blockers and captopril to evaluate the effects of ACEi in the management of IH.

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**Website:** www.ijdvl.com

**DOI:** 10.4103/0378-6323.110809